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BRIEF REPORT

Nephrotic-range proteinuria in an eight-year-old traveler with severe dengue: Case report and review of the literature

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Summary We report a case of an eight-year-old male, native of the Dominican Republic, who visited the U.S. and was admitted to a pediatric intensive care unit with severe dengue. He needed aggressive fluid management for dengue shock syndrome and developed proteinuria on the sixth day of his illness, shortly after his nadir thrombocytopenia. His proteinuria peaked on the eight day, and reduced to trace levels by the tenth day of his illness, coinciding with normalization of his platelet count. His highest random urine protein/creatinine ratio was in the nephrotic range, at 3.9 g/g. Dengue fever can cause a wide spectrum of acute kidney injury (AKI), ranging in incidence from 0.9 to 36%. Review of the literature shows that nephrotic-range proteinuria is an uncommon complication of AKI caused by dengue, reported thus far only in Southeast Asia. Immune-mediated mechanisms may explain the observed association between dengue-induced thrombocytopenia and severe proteinuria, in this case, and previously reported cases. Dengue virus infection is the commonest mosquito-borne disease in the world with substantial morbidity and mortality. Well-designed prospective studies are needed to further characterize the extent and mechanisms of AKI in populations living in countries with ongoing transmission, as well as in those with travel-associated disease.

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1. Introduction

Dengue virus infection is prevalent in tropical and subtropical countries world-wide [1]. The spectrum of disease can vary, ranging from an asymptomatic infection through dengue, dengue with warning signs, and a severe infection with organ involvement, plasma leakage and/or hemorrhage [2]. Acute kidney injury (AKI) following dengue is well documented in the literature. It comprises a heterogeneous collection of disorders such as acute tubular necrosis, glomerulonephritis, proteinuria, nephrotic syndrome, hemolytic uremic syndrome and rhabdomyolysis that have not been studied in a systematic manner [3]. Where histology has been performed, acute tubular necrosis, thrombotic microangiopathy and acute glomerulonephritis were described [4–8]. The incidence of AKI in dengue has ranged from 0.9% to 35.7% depending on the population studied, the criteria for the diagnosis of AKI used, and the severity of dengue [3]. The majority of dengue cases in the U.S. occur in travelers to countries with endemic disease, presenting as an acute non-specific febrile illness within 14 days of their return [9]. We have previously described a case series of children with dengue infection who were admitted to an inner-city community hospital in the South/Central Bronx, New York with dengue, all of whom had returned from a trip to destinations in the Caribbean where they were visiting friends and relatives [10]. In this report we describe an eight-year-old autistic child who lives in the Dominican Republic and was visiting the U.S. when he was admitted at our institution with severe secondary dengue infection, and subsequently developed massive proteinuria which resolved spontaneously.

2. Case report

An eight-year-old male, native of the Dominican Republic, was visiting the U.S. and brought to the pediatric emergency department (ED) with a one day history of fever and malaise, accompanied by rigors and a frontal headache (first day of his illness). He was discharged with a diagnosis of viral syndrome, experienced temporary improvement with antipyretics, but returned back to the ED two days later with persistent fever and persistent non-bloody, non-bilious vomiting. His past medical history was significant for autistic spectrum disorder and one episode of uncomplicated urinary tract infection. Apart from a temperature of 103.3° F (39.6° C) and new onset of petechiae in both lower extremities at the second visit, his physical exam was unremarkable. Initial work up performed in the ED (third day of his illness) revealed a leucocyte count of 5300 cells/μL, an absolute neutrophil count of 3800 cells/μL and a platelet count of 97,000 cells/μL. His electrolytes and liver function test were normal and a blood smear for malaria parasites was negative. He was admitted and started on intravenous ceftriaxone. Dengue-specific serology sent from the floor at this point showed an IgG enzyme-linked immunosorbent assay expressed as an index value of 5.28 (normal range: <0.90) and IgM index value of 0.24 (normal range: <0.90), indicative of a past dengue infection. He continued having daily fever spikes, up to 103.8° F (39.9° C) over the first two days of his hospitalization and repeat blood smear for malaria parasites, two consecutive blood cultures and urine cultures were negative. Daily complete blood counts showed worsening leucopenia and neutropenia, with a nadir of 2400 and 800 cells/μL respectively, along with hyponatremia (128 mmol/L), hypokalemia (2.7 mmol/L) and a platelet count of 22,000 cells/μL on the fourth day of illness. He was transferred to the pediatric intensive care unit for closer monitoring due to borderline systolic blood pressures and poor urine output, and received two boluses of normal saline, and subsequent aggressive fluid management. Petechiae were now noted on his face in addition to his lower extremities. The following day, he had developed hypoalbuminemia (2.6 g/dL) and hypoproteinemia (4.5 g/dL) and a nadir platelet count of 16,000 cells/μL. That night he had two episodes of hematemesis and was transfused with a unit of single donor platelets. Additionally, he received a second unit of platelets on the sixth day of his illness, at which point a urine dipstick, which was negative previously (on the third day of day illness), was positive for protein at 75 mg/mL (normal: negative or trace, <30 mg/mL). On day seven his partial thromboplastin time was 44.6 s (normal range: 26.1–33.8 s), his prothrombin time was slightly elevated (international normalized ratio of 1.2) and he received a fresh frozen plasma transfusion and vitamin K. He had a proteinuria of 150 mg/dL on dipstick and a random spot urine protein/creatinine ratio (UPC) of 3.9 g/g, with cholesterol and triglycerides levels within normal limits. Overnight he was noted to have dullness to percussion with reduced air entry on the right hemi thorax, and chest x-ray confirmed a moderate-sized right pleural effusion with underlying atelectasis. On day eight he received intravenous 25% albumin with furosemide and had a dipstick proteinuria of 500 mg/dL with a random UPC of 3.3 g/g. Repeat dengue testing now showed an increase in his IgG index value to 8.67, and appearance of IgM antibodies, with a value of 1.32, confirming acute secondary dengue infection. His proteinuria declined on days nine and 10 of his illness to 150 mg/dL (UPC of 1 g/g) and trace (UPC of 0.3 g/g) respectively (Fig. 1). On day six his leucopenia and neutropenia resolved and by day nine his thrombocytopenia had also resolved. His urine microscopies were all negative for red blood cells, white blood cells and casts. RNA RT-PCR performed prior to discharge on day 10 of his illness was

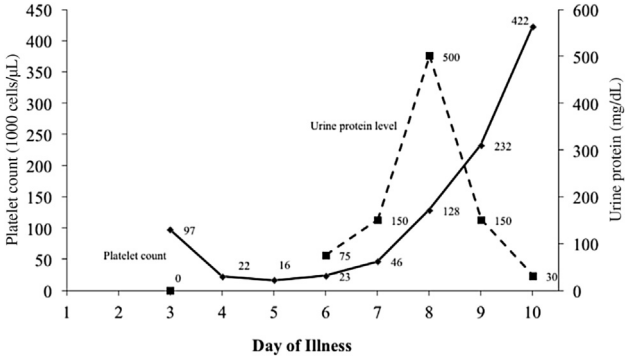

Fig. 1 Dynamics of platelet count and urine proteinuria in an 8-year-old traveler with severe dengue complicated by nephrotic-range proteinuria.